



Does ethnicity matter in chemotherapy for breast cancer?

Andrzej L. Komorowski¹, Maksymilian Kruczala²

¹Chair of Surgery, Andrzej Frycz Modrzewski Krakow University, Krakow, Poland; ²Medical Oncology Department, Chrzanow County Hospital, Chrzanow, Poland

Correspondence to: Andrzej L. Komorowski, MD, PhD. Andrzej Frycz Modrzewski Krakow University, Krakow, Poland. Email: z5komoro@cyf-kr.edu.pl.

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The efficacy of pertuzumab with docetaxel in neoadjuvant treatment of HER2 positive breast cancer patients has been proven in NEOSPHERE trial (1). However, since only 25% of patients participating in that trial had Asian origins, it is not completely safe to extrapolate its results to Asian population. It has been shown that ethnic differences in toxicity profile exist between Asian and Caucasian patients given adjuvant docetaxel and cyclophosphamide. And since those differences can reach important numbers (e.g., grade ≥ 3 neutropenia in 5% of Caucasians and 30% of Asians) (2), we have to be cautious while implementing results of one trial to another population (3).

The PEONY trial fills therefore an important data gap giving us the results of double-blind phase III trial of efficacy and safety of pertuzumab and docetaxel in Asian patients with early and locally advanced breast cancer (4).

The compared treatment regimens in PEONY trial were similar to two of the four arms of the NEOSPHERE trial with one important difference: pertuzumab was given also in postoperative period. The primary endpoint was complete pathologic response (ypT0/ypTis, ypTN0) evaluated in surgical specimen of operated patients by an independent commission.

The independent specimen evaluation is one of the strongest aspects of the PEONY trial: it has not been used in the NEOSPHERE trial. On the other hand, some data from experimental arm require further analysis: adverse events grade 3 and up occurred in 48.6%, diarrhea was fairly common (38.5%) and grade 2 severe diarrhea occurred in every tenth patient. There was one death in the experimental arm due to a suicide; the authors state that it

was not related to pertuzumab, trastuzumab or docetaxel treatment but the effects on those treatments on the occurrence of suicidal thoughts is not well studied.

The primary endpoint of the PEONY trial was not clinically relevant. While complete pathologic response most probably translates into long-term benefit for the patient, we still don't know if it does for sure. Unfortunately, the PEONY trial was not powered enough to provide us with survival data after longer follow-up. Nevertheless, we have to wait for clear evidence of long-term survival benefit for breast cancer patients from all races in order to be able to expose our patients to all the complications related to the combined treatment evaluated in the PEONY trial.

As stated before, extrapolating toxicities from chemotherapy across ethnicities is difficult or even not possible (5) and emphasizing the need to validate safety of chemotherapeutic regimens in patients of different ethnicities.

The results of PEONY trial stay in line with result of the NEOSPHERE trial and constitute therefore a strong argument for combining pertuzumab with docetaxel in breast cancer patients also in Asian population. For a definitive argument in favor, we'll have to wait to see clear survival benefit.

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